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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,912	10/08/2004	Osvaldo A Flores	21080P	6208
210	7590	03/26/2008	EXAMINER	
MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER			
			1648	
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			03/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.	Applicant(s)	
10/510,912	FLORES ET AL.	
Examiner	Art Unit	
Zachariah Lucas	1648	

—The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

THE REPLY FILED 04 March 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires ____ months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on 04 March 2008. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) They raise the issue of new matter (see NOTE below);
 (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) ____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 21,39-41 and 43.

Claim(s) objected to: _____.

Claim(s) rejected: 19,20,28,29 and 31-38.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fail to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: The objection to claims 21 and 39-43 is withdrawn.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648

Continuation of 11. does NOT place the application in condition for allowance because: The Applicant traverses the rejection of claims 19-20, 28-29, 31-34, and 37-38 over the teachings of De Francesco, Rice I and II, and Li; and of claims 35 and 36 over these references further in view of Hawkins, on several grounds.

The Applicant first presents three arguments directed to the teachings of De Francesco and Rice I relating to the use of HCV 3' UTR sequences.

The Applicant begins with an assertion that a disclosure of a genus fails to render obvious a species of that genus. With respect to this argument it is noted that the combined teachings of the cited references not only render obvious the genus, but also, through the teachings of Rice I identifying several HCV 3'UTR sequences, render obvious specific species of that genus including the one being claimed. In each of the decisions cited by the Applicant, the finding that a genus did not render the species obvious related to situations wherein the claimed species was not specifically disclosed. As the present case varies from the facts of the cited decisions, and as the combined teachings in the art would render obvious both the genus and the claimed species, the Applicant's argument is not found persuasive.

With respect to Rice I, the Applicant asserts that the teachings of the reference do not indicate that HCV-1a sequences are any better than those of other strains. While this may be the case, the combined teachings of the art indicate that any HCV UTR may be used. Because Rice I teaches the sequences of several HCV UTR sequences, including the 3' UTR of HCV 1a, it would have been obvious to those of ordinary skill in the art to use any of these sequences, including that of HCV 1a. Thus, Applicant's argument with respect to the teachings of Rice I are not found persuasive.

Finally, the Applicants asserts that the teachings of De Francesco fail to demonstrate that the con-1 and 1a sequences are equivalents. The Applicant's arguments are not found persuasive. The teachings of the reference, as noted by the Applicant, indicate that any naturally occurring or functionally equivalent HCV 3' UTR may be used. This statement clearly implies that those in the art may use any such UTR's in the making of HCV replicons. As such, it would have been obvious to those of ordinary skill in the art that the various HCV 3' UTR sequences disclosed by Rice I could be used as functional equivalents in the making of HCV replicons. The Applicant's argument is therefore not found persuasive.

The Applicant next asserts that the teachings of Melnick and Li fail to teach the use of sequence from clinical isolates in HCV replicons. These arguments are not found persuasive for the reasons indicated in the prior actions. It is again noted that the Applicant failed to consider the teachings of the WO 01/89364 reference. The Applicant also asserts that the identification of a problem is not tantamount to solving that problem. However, while this may be the case, a mode for solving this problem was suggested by the teachings in the prior art as indicated in the action mailed on July 9, 2007 (pages 6-7). Moreover, because the Examiner relied on teachings in the art to show the motivation, the Examiner disagrees that improper hindsight has been applied. In view of the above, the Applicant's argument is not found persuasive.

Applicant's assertion that the claimed replicons were not actually made by any of the cited references is also not found persuasive. This is not an anticipation rejection where it must be shown that each of the claim limitations are met by a single reference. This is an obviousness rejection showing that the claimed invention would have been obvious to those of ordinary skill in the art based on the teachings of cited references. The fact that the Applicant may have been the first to actually make such replicons is not relevant to the determination as to whether it would have been obvious for those in the art to have made them.

IThe Applicant traverses the rejection of claims 19-20, 28, 29, 31-34, 37 and 38 over claims 9 and 10 of copending application 10/543633. The traversal is on the grounds that the claims were amended to refer only to SEQ ID NO: 1 of that application, and that the replicon of that sequence does not contain an HCV 1a 3' UTR or a portion from a clinical isolate. It is noted that, while claims 9 and 10 of the copending application have been amended as indicated by the Applicant, additional claims 19 and 20 of that application have been added which read on the second replicon previously described by claims 9 and 10. Further, contrary to Applicant's assertion on page 11 of the After-Final Response, it is noted that page 10 of the copending application indicates that the replicons of copending claims 10 and (newly added) 20 (comprising SEQ ID NOs: 3 and 4, respectively) each includes an HCV 1a 3'UTR. The paragraphs referred to by the Applicant on page 11 of the After-Final response do not teach otherwise. Paragraph 24 indicates that the NS3-NS5B seqiemces were relaced in SEQ ID NO: 1 or 2 of that application. Paragraph 138 does not indicate what sequence is being described, or that the described sequence corresponds to one of the SEQ ID NOs of the application.Further, the reference indicates that the HCV-BK sequences used to make the disclosed replicons were derived from sequences from patients- hence- clincial isolates. Page 16. The rejection is therefore maintained over claims 9, 10, 19, and 20 of the copending application..